EXHIBIT 2

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Order Granting / Denying Request For Ex Parte Reexamination	Control No. 90/007,542	Patent Under Reexamination 6331415	
	Examiner David J. Blanchard	Art Unit 1643	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

The request for *ex parte* reexamination filed *13 May 2005* has been considered and a determination has been made. An identification of the claims, the references relied upon, and the rationale supporting the determination are attached.

Attachments: a)☐ PTO-892, b)☒ PTO-1449, c)☐ Other: _____

1. ☒ The request for *ex parte* reexamination is GRANTED.

RESPONSE TIMES ARE SET AS FOLLOWS:

For Patent Owner's Statement (Optional): TWO MONTHS from the mailing date of this communication (37 CFR 1.530 (b)). **EXTENSIONS OF TIME ARE GOVERNED BY 37 CFR 1.550(c).**

For Requester's Reply (optional): TWO MONTHS from the **date of service** of any timely filed Patent Owner's Statement (37 CFR 1.535). **NO EXTENSION OF THIS TIME PERIOD IS PERMITTED.** If Patent Owner does not file a timely statement under 37 CFR 1.530(b), then no reply by requester is permitted.

2. ☐ The request for *ex parte* reexamination is DENIED.

This decision is not appealable (35 U.S.C. 303(c)). Requester may seek review by petition to the Commissioner under 37 CFR 1.181 within ONE MONTH from the mailing date of this communication (37 CFR 1.515(c)). **EXTENSION OF TIME TO FILE SUCH A PETITION UNDER 37 CFR 1.181 ARE AVAILABLE ONLY BY PETITION TO SUSPEND OR WAIVE THE REGULATIONS UNDER 37 CFR 1.183.**

In due course, a refund under 37 CFR 1.26 (c) will be made to requester:

a) ☐ by Treasury check or,

b) ☐ by credit to Deposit Account No. _____, or

c) ☐ by credit to a credit card account, unless otherwise notified (35 U.S.C. 303(c)).

cc:Requester (if third party requester)

DECISION GRANTING EX PARTE REEXAMINATION

A substantial new question of patentability affecting claims 1-36 of United States Patent 6,331,415 to Cabilly et al is raised by the present request for inter partes reexamination.

Extensions of time under 37 CFR 1.136(a) will not be permitted in *inter partes* reexamination proceedings because the provisions of 37 CFR 1.136 apply only to "an applicant" and not to the patent owner in a reexamination proceeding. Additionally, 35 U.S.C. 314(c) requires that *inter partes* reexamination proceedings "will be conducted with special dispatch" (37 CFR 1.937). Patent owner extensions of time in *inter partes* reexamination proceedings are provided for in 37 CFR 1.956. Extensions of time are not available for third party requester comments, because a comment period of 30 days from service of patent owners response is set by statute. 35 U.S.C. 314(b)(3).

The patent owner is reminded of the continuing responsibility under 37 CFR 1.565(a) to apprise the Office of any litigation activity, or other prior or concurrent proceeding, involving U.S. Patent No. 6,331,415 ('415) throughout the course of this reexamination proceeding. The third party requester is also reminded of the ability to similarly apprise the Office of any such activity or proceeding throughout the course of this reexamination proceeding. See MPEP §§ 2207, 2282 and 2286.

Obviousness-Type Double Patenting

The request indicates that the third party requestor considers claims 1-36 of the '415 patent are unpatentable under the doctrine of obviousness-type double patenting over claims 1-7 of U.S. Patent 4,816,567 ('567).

A. The request indicates that the third party requester considers claims 1, 13, 21 and 33 of the '415 patent as unpatentable under the judicially created doctrine of obviousness-type double patenting over claim 1 of the '567 patent.

It is agreed that the consideration of the '567 patent raises a substantial new question of patentability as to claims 1, 13, 21 and 33 of the '415 patent. As pointed out on pages 40-42 of the request, the '567 and '415 patents include claims directed to the same statutory subject matter: recombinant processes, vectors, and host cells for making immunoglobulins (particularly chimeric immunoglobulins). As pointed out on page 41, claim 1 of the '567 patent is narrower than claims 1, 21 and 33 of the '415 patent because '567 claim 1 is directed to "chimeric" immunoglobulin chains, whereas the immunoglobulin molecules and immunologically functional fragments of claims 1, 21 and 33 of the '415 patent, while reading on the chimeric immunoglobulin chains of the '567 claim, need not be chimeric. The '567 patent essentially claims a species of the immunoglobulin genus claimed in the later '415 patent, which makes '415 patent claims 1, 21 and 33 obvious variants of the '567 patent claim 1. As pointed out on page 40, a second application containing a broader claim, more generic in character that the specific claim in the prior patent, typically cannot support a valid, independent patent.

(i.e., species anticipates the genus). As pointed out on page 41, the same applies for the vector (claims 5) and host cell (claim 7) claims of the '567 patent and the corresponding claims 15 and 16 (vector) and 17, 18 and 20 (host cell) of the '415 patent. As pointed out on page 41, claim 1 of the '567 patent recites a chimeric immunoglobulin species of the sub-genus defined by claim 13 of the '415 patent. As pointed out on page 42, claims 2, 4, and 6 of the '567 patent are directed to a human constant region of the chimeric immunoglobulin, which is another example of example of a species within the genus claimed in the '415 patent.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider the claims of the '567 patent important in deciding whether or not the claims are patentable. Accordingly, the claims of the '567 patent raises a substantial new question of patentability as to claims 1, 13, 21 and 33, which question has not been decided in a previous examination of the '415 patent.

B. The request indicates that dependent claims 2, 3 and 25 are obvious over claim 1 of the '567 patent in view of Axel (U.S. Patent No. 4,399,216, Ids filed 5/13/2005) because claim 1 of the '567 patent reads on the process involving each of different vectors and Axel teaches transformed mammalian cells that produce multiple heterologous proteins on different vectors or on the same vector as indicated on page 46 of the request.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 1 of the '567 patent in view of Axel important in deciding whether

or not the claims are patentable. Accordingly, the claim1 of the '567 patent in view of Axel raises a substantial new question of patentability as to claims 2, 3and 25, which question has not been decided in a previous examination of the '415 patent.

C. The request indicates that claims 4-5 are obvious over claim 1 of the '567 patent in view of Axel or Kaplan (EP 0 044 722, Ids filed 5/13/2005) as indicated on page 46 of the request which states that a plasmid, particularly pBR322 is a type of vector within the scope of claim 1 of the '567 patent and Axel and Kaplan both teach the use of plasmids, particularly pBR322 for expressing heterologous proteins.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 1 of the '567 patent in view of Axel and Kaplan important in deciding whether or not the claims are patentable. Accordingly, claim 1 of the '567 patent in view of Axel and Kaplan raises a substantial new question of patentability as to claims 4-5, which question has not been decided in a previous examination of the '415 patent.

D. The request indicates that claims 6-8, 19 and 26 are obvious over claim 1 of the '567 patent in view of Axel, Rice (Proc. Natl. Acad. Sci. USA 79:7862-7865, December 1982, Ids filed 5/13/2005) and/or Kaplan as indicated on pages 46-47 of the request which states Axel teaches mammalian host cells fro expressing proteins, including antibodies and Rice demonstrates expression of a recombinant light chain in a

mammalian host cell and Kaplan teaches bacterial and yeast host cells for expressing recombinant immunoglobulin chains.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 1 of the '567 patent in view of Axel, Rice and/or Kaplan important in deciding whether or not the claims are patentable. Accordingly, claim 1 of the '567 patent in view of Axel, Rice and/or Kaplan raises a substantial new question of patentability as to claims 6-8, 19 and 26 which question has not been decided in a previous examination of the '415 patent.

E. The request indicates that claims 9 and 29 are obvious over claim 1 of the '567 patent in view of Axel and/or Rice as indicated on page 47 of the request which states Axel teaches mammalian host cells fro expressing proteins, including antibodies and Rice demonstrates expression of a recombinant light chain in a mammalian host cell.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 1 of the '567 patent in view of Axel and/or Rice important in deciding whether or not the claims are patentable. Accordingly, claim 1 of the '567 patent in view of Axel and/or Rice raises a substantial new question of patentability as to claims 9 and 29, which question has not been decided in a previous examination of the '415 patent.

F. The request indicates that claims 10, 27, 28 and 31 are obvious over claim 1 of the '567 patent in view of Kaplan and the admitted prior art as indicated on pages 47-48

of the request which states Kaplan teaches bacterial and yeast host cells for expressing recombinant immunoglobulin chains and Kaplan teaches rupturing host cells, isolating the heavy and light chains, and combining them under mildly oxidative conditions to promote refolding and disulfide bond formation.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 1 of the '567 patent in view of Kaplan important in deciding whether or not the claims are patentable. Accordingly, claim 1 of the '567 patent in view of Kaplan raises a substantial new question of patentability as to claims 10, 27, 28 and 31, which question has not been decided in a previous examination of the '415 patent.

G. The request indicates that claims 15-16 are obvious over claim 5 of the '567 patent in view of Axel or Kaplan as indicated on page 48 of the request which states Axel and Kaplan both teach the use of plasmids, particularly pBR322 for expressing heterologous proteins.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 5 of the '567 patent in view of Axel or Kaplan important in deciding whether or not the claims are patentable. Accordingly, claim 5 of the '567 patent in view of Axel and Kaplan raises a substantial new question of patentability as to claims 15-16, which question has not been decided in a previous examination of the '415 patent.

H. The request indicates that claims 18 and 20 are obvious over claim 7 of the '567 patent in view of Axel and Rice, and claim 18 is further an obvious variant of '567 claim

7 in view of Kaplan as indicated on pages 48-49 of the request which states Axel teaches mammalian host cells for expressing proteins, expressly including antibodies and Rice demonstrates expression of a recombinant immunoglobulin light chain in a mammalian host cell and Kaplan teaches bacterial and yeast host cells for expressing recombinant immunoglobulin chains.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 7 of the '567 patent in view of Axel, Rice and Kaplan important in deciding whether or not the claims are patentable. Accordingly, claim 7 of the '567 patent in view of Axel, Rice and Kaplan raises a substantial new question of patentability as to claims 18 and 20, which question has not been decided in a previous examination of the '415 patent.

I. The request indicates that claim 22 is obvious over claim 1 of the '567 patent in view of Accolla et al (Proc. Natl. Acad. Sci. USA 77(1):563-566, January 1980, Ids filed 5/13/2005) or the admitted prior art as indicated on page 49 of the request which states Accolla teaches making anti-CEA monoclonal antibodies and the '415 patentee admits that anti-CEA antibodies are useful for the detection and potentially for use in treatment of tumors that have CEA at their surface (see '415 patent column 16, lines 31-38; particularly the cited art of Gold et al., J. Exp. Med. 122:467, 1965 and Van Nagell et al., Cancer research 40:502, 1980).

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 1 of the '567 patent in view of Accolla or the admitted prior art

important in deciding whether or not the claims are patentable. Accordingly, claim 1 of the '567 patent in view of Accolla or the admitted prior art of Gold et al and Van Nagell et al raises a substantial new question of patentability as to claim 22, which question has not been decided in a previous examination of the '415 patent.

J. The request indicates that claims 23-24 are obvious over claim 1 of the '567 patent in view of Rice or the admitted prior art as indicated on page 49 of the request which states Rice teaches expressing a recombinant kappa chain with an endogenous gamma chain in a host cell to produce an immunoglobulin molecule.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 1 of the '567 patent in view of Rice important in deciding whether or not the claims are patentable. Accordingly, claim 1 of the '567 patent in view of Rice raises a substantial new question of patentability as to claims 23-24, which question has not been decided in a previous examination of the '415 patent.

K. The request indicates that claim 30 is obvious over claim 1 of the '567 patent in view of Kaplan as indicated on pages 49-50 of the request which states Kaplan teaches bacterial host cells for expressing recombinant immunoglobulin chains.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 1 of the '567 patent in view of Kaplan important in deciding whether or not the claims are patentable. Accordingly, claim 1 of the '567 patent in view

of Kaplan raises a substantial new question of patentability as to claim 30, which question has not been decided in a previous examination of the '415 patent.

L. The request indicates that claims 32 is obvious over claim 3 of the '567 patent in view of Kaplan as indicated on page 50 of the request, which states that claim 3 of the '567 patent is directed to a composition comprising a chimeric immunoglobulin heavy or light chain, whether it is soluble or insoluble and Kaplan teaches bacterial and yeast host cells for expressing recombinant immunoglobulin chains.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 3 of the '567 patent in view of Kaplan and the admitted prior art important in deciding whether or not the claims are patentable. Accordingly, claim 3 of the '567 patent in view of Kaplan raises a substantial new question of patentability as to claim 32, which question has not been decided in a previous examination of the '415 patent.

M. The request indicates that claims 34-36 are obvious over claim 1 of the '567 patent in view of Kaplan as indicated on pages 50-51 of the request because Kaplan teaches that an antibody can be used for site directed therapy by directing a drug or other therapeutic means to such site (see page 8, lines 7-21).

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 1 of the '567 patent in view of Kaplan important in deciding whether or not the claims are patentable. Accordingly, claim 1 of the '567 patent in view

of Kaplan raises a substantial new question of patentability as to claims 34-36, which question has not been decided in a previous examination of the '415 patent.

"Schneller-Type" Double Patenting

The request indicates that the third party requestor considers claims 1-10, 13 and 15-33 of the '415 patent be reexamined under the doctrine of non-statutory double patenting based on improper timewise extension of patent rights (referred to as "*Schneller*-type" double patenting) over claims 1-7 of the '567 patent.

N. The request indicates that claims 1, 13, 21 and 33 extend in time the protection afforded by claim 1 of the '567 patent for the production of a chimeric immunoglobulin in a single host cell as indicated on pages 53-54 of the request.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claims 1, 13, 21 and 33 important in deciding whether or not the claims would extend in time the protection afforded by claim 1 of the '567 patent. Accordingly, claims 1, 13, 21 and 33 of the '415 patent raise a substantial new question of a timewise extension of the protection afforded by claim 1 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

O. The request indicates that claims 2, 3 and 25 extend in time the protection afforded by claim 1 of the '567 patent for the production of a chimeric immunoglobulin in a single host cell as indicated on page 54 of the request because claims 3 and 25 recite

that the DNA sequences encoding the heavy and light chains are present in a single vector and claim 1 of the '567 patent reads on the process involving each of different vectors, or both DNAs on the same vector, since the process includes preparing each DNA sequence and inserting it in an expression vector for expression of each of the heavy and light chains before they are assembled into an immunoglobulin.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claims 2, 3 and 25 of the '415 patent important in deciding whether or not the claims would extend in time the protection afforded by claim 1 of the '567 patent. Accordingly, claims 2, 3 and 25 of the '415 patent raise a substantial new question of a timewise extension of the protection afforded by claim 1 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

P. The request indicates that claims 4 and 5 extend in time the protection afforded by claim 1 of the '567 patent for the production of a chimeric immunoglobulin in a single host cell as indicated on page 54 of the request because claim 4 of the '415 patent recites that the vector is a plasmid and claim 5 recites that the plasmid is pBR322 and a plasmid, particularly pBR322 is a type of vector within the scope of claim 1 of the '567 patent.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claims 4 and 5 of the '415 patent important in deciding whether or not the claims would extend in time the protection afforded by claim 1 of the '567 patent. Accordingly, claims 4 and 5 of the '415 patent raise a substantial new question of a

timewise extension of the protection afforded by claim 1 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

Q. The request indicates that claims 6-8, 19 and 26 extend in time the protection afforded by claim 1 of the '567 patent for the production of a chimeric immunoglobulin in a single host cell as indicated on pages 54-55 of the request because claims 6-8, 19 and 26 recite specific types of host cells that are within the scope of claim 1 of the '567 patent.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claims 6-8, 19 and 26 of the '415 patent important in deciding whether or not the claims would extend in time the protection afforded by claim 1 of the '567 patent. Accordingly, claims 6-8, 19 and 26 of the '415 patent raise a substantial new question of a timewise extension of the protection afforded by claim 1 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

R. The request indicates that claims 9-10, 27, 28, 29 and 31 extend in time the protection afforded by claim 1 of the '567 patent for the production of a chimeric immunoglobulin in a single host cell as indicated on page 55 of the request because claims 9-10, 27, 28, 29 and 31 are drawn to methods wherein prior to formation of the immunoglobulin, one produces each of the heavy and light chains as separate molecules.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claims 9-10, 27, 28, 29 and 31 of the '415 patent important in deciding whether or not the claims would extend in time the protection afforded by claim 1 of the '567 patent. Accordingly, claims 9-10, 27, 28, 29 and 31 of the '415 patent raise a substantial new question of a timewise extension of the protection afforded by claim 1 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

S. The request indicates that claims 15 and 16 extend in time the protection afforded by claim 5 of the '567 patent for a vector comprising a DNA sequence encoding a chain or chains of a chimeric immunoglobulin in a single host cell as indicated on page 55 of the request because claims 15 and 16 include sequences encoding chimeras and claim 5 of the '567 patent includes a vector that includes DNA encoding both a chimeric immunoglobulin heavy chain and light chain.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claims 15 and 16 of the '415 patent important in deciding whether or not the claims would extend in time the protection afforded by claim 5 of the '567 patent. Accordingly, claims 15 and 16 of the '415 patent raise a substantial new question of a timewise extension of the protection afforded by claim 5 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

T. The request indicates that claims 18 and 20 extend in time the protection afforded by claim 7 of the '567 patent for host cells containing a vector for the production of a chimeric immunoglobulin in a single host cell as indicated on page 56 of the request because claims 18 and 20 include sequences encoding chimeras and claim 7 of the '567 patent for host cells containing a vector for the production of a chimeric immunoglobulin in a single host cell.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claims 18 and 20 of the '415 patent important in deciding whether or not the claims would extend in time the protection afforded by claim 7 of the '567 patent. Accordingly, claims 18 and 20 of the '415 patent raise a substantial new question of a timewise extension of the protection afforded by claim 7 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

U. The request indicates that claim 22 extends in time the protection afforded by claim 1 of the '567 patent for the production of a chimeric anti-CEA immunoglobulin in a single host cell as indicated on page 56 of the request because claim 22 limits the method of claim 21 to making an anti-CEA antibody and CEA is a specific antigen within the general scope of a "particular known antigen" of claim 1 of the '567 patent.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 22 of the '415 patent important in deciding whether or not the claims would extend in time the protection afforded by claim 1 of the '567 patent. Accordingly, claim 22 of the '415 patent raise a substantial new question of a timewise

extension of the protection afforded by claim 1 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

V. The request indicates that claims 23 and 24 extend in time the protection afforded by claim 1 of the '567 patent for the production of a chimeric immunoglobulin in a single host cell as indicated on page 56 of the request because claim 23 limits the method of claim 21 to that in which the heavy chain is of the gamma family and claims 24 limits the method of claim 21 to that which the light chain is of the kappa family, which are within the scope of the "heavy chain" and "light chain" of claim 1 of the '567 patent.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claims 23 and 24 of the '415 patent important in deciding whether or not the claims would extend in time the protection afforded by claim 1 of the '567 patent. Accordingly, claims 23 and 24 of the '415 patent raise a substantial new question of a timewise extension of the protection afforded by claim 1 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

W. The request indicates that claim 30 extends in time the protection afforded by claim 1 of the '567 patent for the production of a chimeric immunoglobulin in a single host cell as indicated on pages 56-57 of the request because claim 30 recites that the host cell is a gram negative bacteria and the heavy and light chains are secreted into

the periplasmic space of the host cell and gram negative bacterium, such as *E. coli* is a host cell within the scope of claim 1 of the '567 patent.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 30 of the '415 patent important in deciding whether or not the claims would extend in time the protection afforded by claim 1 of the '567 patent. Accordingly, claim 30 of the '415 patent raise a substantial new question of a timewise extension of the protection afforded by claim 1 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

X. The request indicates that claim 32 extends in time the protection afforded by claim 3 of the '567 patent for insoluble chimeric heavy and/or light chain compositions as indicated on page 57 of the request because claim 32 is directed to a composition of matter comprising immunoglobulin proteins and claim 3 of the '567 patent is directed to a composition comprising a chimeric immunoglobulin heavy or light chain, whether it is soluble or insoluble.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider claim 32 of the '415 patent important in deciding whether or not the claims would extend in time the protection afforded by claim 3 of the '567 patent. Accordingly, claim 32 of the '415 patent raise a substantial new question of a timewise extension of the protection afforded by claim 3 of the '567 patent, which question has not been decided in a previous examination of the '415 patent.

All correspondence relating to this *Ex parte* reexamination proceeding should be directed:

By Mail to: Mail Stop *Ex Parte* Reexam
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By FAX to: (571) 273-0100
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By hand: Customer Service Window
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Any inquiry concerning this communication or earlier communications from the examiner, or as to the to the status of this proceeding, should be directed to the Central Reexamination Unit at telephone number (703) 308-9692.

David Blanchard
Art Unit 1643

LARRY R. HELMS, PH.D
PRIMARY EXAMINER